

SEQUENCE LISTING

Zhou, Ming-Ming Aggarwal, Aneel

<120> Methods of Identifying Modulators of Bromodomains

<130> 2459-1-003

<140> 09/510,314

<141> 2000-02-22

<160> 44

<170> PatentIn version 3.0

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Gln Tyr Gln Glu Pro Trp Gln Tyr Val Asp Asp Val Trp Leu Met Phe 80

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Pro Val Asp Pro Gln Leu Leu Gly Ile Pro Asp Tyr Phe Asp Ile Val 35 40 45

Lys Asn Pro Met Asp Leu Ser Thr Ile Lys Arg Lys Leu Asp Thr Gly 50 60

Gln Tyr Gln Glu Pro Trp Gln Tyr Val Asp Asp Val Arg Leu Met Phe 70 75 80

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Arg Pro Met Asp Leu Glu Thr Val His Lys Lys Leu Tyr Ala Gly Gln 50 60

Tyr Gln Asn Ala Gly Gln Phe Cys Asp Asp Ile Trp Leu Met Leu Asp 65 70 75 80

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Pro Ser Arg Glu Glu Phe Arg Glu His Leu Glu Leu Ile Val Lys Asn 70 75 80

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Met Asp Leu Ser Thr Ile Glu Arg Lys Leu Asn Val Gly Ala Tyr Glu 50 60

Val Pro Glu Gln Ile Thr Glu Asp Phe Asn Leu Met Val Asn Asn Ser 65 70 75 80

Ile Lys Phe Asn Gly Pro Asn Ala Gly Ile Ser Gln Met Ala Arg Asn $85 \hspace{1cm} 90 \hspace{1cm} 95$

Ile Gln Ala Ser Phe Glu Lys His Met Leu Asn Met Pro 100 105

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<211> 113

<212> PRT

<213> Homo sapiens

<400> 23

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Lys Pro Val Asp Ala Ser Ala Leu Gly Leu His Asp Tyr His Asp Ile 35 40 45

Ile Lys His Pro Met Asp Leu Ser Thr Val Lys Arg Lys Met Glu Asn 50 60

Arg Asp Tyr Arg Asp Ala Gln Glu Phe Ala Ala Asp Val Arg Leu Met 65 70 75 80

Phe Ser Asn Cys Tyr Lys Tyr Asn Pro Pro Asp His Asp Val Val Ala 85 90 95

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<212> PRT

<213> Homo sapiens

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Ile Lys His Pro Met Asp Leu Ser Thr Val Lys Arg Lys Met Asp Gly 50 60

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<212> PRT

<213> Drosophila melanogaster

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Lys Ser Lys Arg Leu Gln Gln Ala Met Lys Phe Cys Gln Ser Val Leu 1 5 10 15

Lys Glu Leu Met Ala Lys Lys His Ala Ser Tyr Asn Tyr Pro Phe Leu 20 25 30

Glu Pro Val Asp Pro Val Ser Met Asn Leu Pro Thr Tyr Phe Asp Tyr 35 40 45

Val Lys Glu Pro Met Asp Leu Gly Thr Ile Ala Lys Lys Leu Asn Asp 50 55 60

Trp Gln Tyr Gln Thr Met Glu Asp Phe Glu Arg Glu Val Arg Leu Val 65 70 75 80

Phe Lys Asn Cys Tyr Thr Phe Asn Pro Asp Gly Thr Ile Val Asn Met 85 90 95

Met Gly His Arg Leu Glu Glu Val Phe Asn Ser Lys Trp Ala Asp Arg $100 \hspace{1cm} 105 \hspace{1cm} 110$

Pro

<210> 27

<211> 108

<212> PRT

<213> Homo sapiens

<400> 27

Met Glu Met Gln Leu Thr Pro Phe Leu Ile Leu Leu Arg Lys Thr Leu 1 10 15

Glu Gln Leu Gln Glu Lys Asp Thr Gly Asn Ile Phe Ser Glu Pro Val 20 25 30

Pro Leu Ser Glu Val Pro Asp Tyr Leu Asp His Ile Lys Lys Pro Met 35 40 45

Asp Phe Phe Thr Met Lys Gln Asn Leu Glu Ala Tyr Arg Tyr Leu Asn 50 60

Phe Asp Asp Phe Glu Glu Asp Phe Asn Leu Ile Val Ser Asn Cys Leu 65 70 75 80

Lys Tyr Asn Ala Lys Asp Thr Ile Phe Tyr Arg Ala Ala Val Arg Leu Page 15

95

Arg Glu Gln Gly Gly Ala Val Val Arg Gln Ala Arg 100 105

85

<210> 28

<211> 113

<212> PRT

<213> Homo sapiens

<400> 28

Ser Glu Asp Gln Glu Ala Ile Gln Ala Gln Lys Ile Trp Lys Lys Ala 1 10 15

Ile Met Leu Val Trp Arg Ala Ala Ala Asn His Arg Tyr Ala Asn Val 20 25 30

Phe Leu Gln Pro Val Thr Asp Asp Ile Ala Pro Gly Tyr His Ser Ile 35 40 45

Val Gln Arg Pro Met Asp Leu Ser Thr Ile Lys Lys Asn Ile Glu Asn 50 60

Gly Leu Ile Arg Ser Thr Ala Glu Phe Gln Arg Asp Ile Met Leu Met 65 70 75 80

Phe Gln Asn Ala Val Met Tyr Asn Ser Ser Asp His Asp Val Tyr His 85 90 95

Met Ala Val Glu Met Gln Arg Asp Val Leu Glu Gln Ile Gln Gln Phe 100 105 110

Leu

<210> 29

<211> 106

<212> PRT

<213> Gallus gallus

<400> 29

Asn Leu Pro Thr Val Asp Pro Ile Ala Val Cys His Glu Leu Tyr Asn 1 5 10 15

Thr Ile Arg Asp Tyr Lys Asp Glu Gln Gly Arg Leu Leu Cys Glu Leu 20 25 30

Phe Ile Arg Ala Pro Lys Arg Arg Asn Gln Pro Asp Tyr Tyr Glu Val 35 40 45

Val Ser Gln Pro Ile Asp Leu Met Lys Ile Gln Gln Lys Leu Lys Met 50 55 60

Glu Glu Tyr Asp Asp Val Asn Val Leu Thr Ala Asp Phe Gln Leu Leu 65 70 75 80

Phe Asn Asn Ala Lys Ala Tyr Tyr Lys Pro Asp Ser Pro Glu Tyr Lys 85 90 95

Ala Ala Cys Lys Leu Trp Glu Leu Tyr Leu 100 105

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<210> 30
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<213> Gallus gallus

<400> 30

Ser Ser Pro Gly Tyr Leu Lys Glu Ile Leu Glu Gln Leu Leu Glu Ala 1 5 10 15

Val Ala Val Ala Thr Asn Pro Ser Gly Arg Leu Ile Ser Glu Leu Phe 20 25 30

Gln Lys Leu Pro Ser Lys Val Gln Tyr Pro Asp Tyr Tyr Ala Ile Ile 35 40 45

Lys Glu Pro Ile Asp Leu Lys Thr Ile Ala Gln Arg Ile Gln Asn Gly
50 60

Thr Tyr Lys Ser Ile His Ala Met Ala Lys Asp Ile Asp Leu Leu Ala 65 70 75 80

Lys Asn Ala Lys Thr Tyr Asn Glu Pro Gly Ser Gln Val Phe Lys Asp 85 90 95

Ala Asn Ala Ile Lys Lys Ile Phe Asn Met Lys Lys Ala Glu Ile Glu $100 \hspace{1cm} 105 \hspace{1cm} 110$

<400> 31

Thr Ser Phe Met Asp Thr Ser Asn Pro Leu Tyr Gln Leu Tyr Asp Thr 10 15

Val Arg Ser Cys Arg Asn Asn Gln Gly Gln Leu Ile Ser Glu Pro Phe 20 25 30

Phe Gln Leu Pro Ser Lys Lys Lys Tyr Pro Asp Tyr Tyr Gln Gln Ile 35 40 45

Lys Thr Pro Ile Ser Leu Gln Gln Ile Arg Ala Lys Leu Lys Asn His 50 60

Glu Tyr Glu Thr Leu Asp Gln Leu Glu Ala Asp Leu Asn Leu Met Phe 65 70 75 80

Glu Asn Ala Lys Arg Tyr Asn Val Pro Asn Ser Ala Ile Tyr Lys Arg 85 90 95

Val Leu Lys Met Gln Gln Val Met Gln Ala Lys Lys Glu Leu Ala 100 105 110

<211> 112

<212> PRT

<210> 31

<211> 112

<212> PRT

<213> Gallus gallus

<210> 32

<211> 113

<212> PRT

<213> Gallus gallus

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<400> 32
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Ser Lys Lys Asn Met Arg Lys Gln Arg Met Lys Ile Leu Tyr Asn Ala Val Leu Glu Ala Arg Glu Ser Gly Thr Gln Arg Arg Leu Gys Asp Leu Met Met Val Lys Pro Ser Lys Lys Asp Tyr Pro Asp Tyr Tyr Lys Ile Leu Glu Pro Met Asp Leu Lys Met Ile Glu His Asn Ile Arg Asn Asp Esp Lys Tyr Val Gly Glu Glu Ala Met Ile Asp Asp Met Lys Leu Met 80 Phe Arg Asn Ala Arg His Tyr Asn Glu Glu Gly Ser Gln Val Tyr Asn 95 Asp Ala His Met Leu Glu Lys Ile Leu Lys Glu Lys Glu Lys Arg Lys Glu Leu Gly

<210> 33 <211> 115 <212> PRT

<213> Gallus gallus

<400> 33

Lys Lys Ser Lys Tyr Met Thr Pro Met Gln Gln Lys Leu Asn Glu Val $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Tyr Glu Ala Val Lys Asn Tyr Thr Asp Lys Arg Gly Arg Arg Leu Ser 20 25 30

Ala Ile Phe Leu Arg Leu Pro Ser Arg Ser Glu Leu Pro Asp Tyr Tyr 35 40 45

Met Ala Asn Lys Tyr Gln Asp Ile Asp Ser Met Val Glu Asp Phe Val 65 70 75 80

Met Met Phe Asn Asn Ala Cys Thr Tyr Asn Glu Pro Glu Ser Leu Ile 85 90 95

Tyr Lys Asp Ala Leu Val Leu His Lys Val Leu Leu Glu Thr Arg Arg 100 105 110

Glu Ile Glu 115

<210> 34

<211> 112

<212> PRT <213> Unknown

His Asn Ala Pro She Asp Lys Thr Lys Phe Asp Glu Val Leu Glu Ala Leu Val Gly Leu Lys Asp Asn Glu Gly Asn Pro Phe Asp Asp Ile Phe Glu Glu Glu Leu Pro Ser Lys Arg Tyr Phe Pro Asp Tyr Tyr Gln Ile Ile Gln Lys Pro Ile Cys Tyr Lys Met Met Arg Asn Lys Ala Lys Thr Gly Sor Tyr Leu Ser Met Gly Asp Phe Tyr Asp Asp Ile Arg Leu Met Val 80 Ser Asn Ala Gln Thr Tyr Asn Met Pro Gly Ser Leu Val Tyr Glu Cys

Ser Val Leu Ile Ala Asn Thr Ala Asn Ser Leu Glu Ser Lys Asp Gly 100 105 110

<400> 35

Gly Thr Asn Glu Ile Asp Val Pro Lys Val Ile Gln Asn Ile Leu Asp Ile Asp Ile Asp Ile Asp Ile Gln Asn Ile Leu Asp Ile Ala Leu His Glu Glu Lys Asp Glu Gln Gly Arg Phe Leu Ile Asp Ile Phe Ile Asp Leu Pro Ser Lys Arg Leu Tyr Pro Asp Tyr Tyr Glu Ile Lys Ser Pro Met Thr Ile Lys Met Leu Glu Lys Arg Phe Lys Lys Gly Glu Tyr Thr Thr Leu Glu Ser Phe Val Lys Asp Leu Asn Gln Met Roll Phe Ile Asn Ala Lys Thr Tyr Asn Ala Pro Gly Ser Phe Val Tyr Glu Asp Asp Ala Glu Lys Leu Ser Gln Leu Ser Ser Ser Leu Ile Ser Ser Phe Asp Phe Ile Ser Ser Phe Ser P

Ser

<210> 35 <211> 113 <212> PRT

<213> Unknown

<220> <223> Description of Unknown Organism: see Jeanmougin et al., Trends in Biochem. Sci. 22:151-153 (1997)

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<210> 36
<211> 113
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<212> PRT

<213> Homo sapiens

<400> 36

Gly Thr Asn Glu Ile Asp Val Pro Lys Val Ile Gln Asn Ile Leu Asp 1 10 15

Ala Leu His Glu Glu Lys Asp Glu Gln Gly Arg Phe Leu Ile Asp Ile $20 \hspace{1cm} 25 \hspace{1cm} 30$

Phe Ile Asp Leu Pro Ser Lys Arg Leu Tyr Pro Asp Tyr Tyr Glu Ile 35 40 45

Ile Lys Ser Pro Met Thr Ile Lys Met Leu Glu Lys Arg Phe Lys Lys 50 60

Gly Glu Tyr Thr Thr Leu Glu Ser Phe Val Lys Asp Leu Asn Gln Met 65 70 75 80

Phe Ile Asn Ala Lys Thr Tyr Asn Ala Pro Gly Ser Phe Val Tyr Glu 85 90 95

Asp Ala Glu Lys Leu Ser Gln Leu Ser Ser Ser Leu Ile Ser Ser Phe $100 \hspace{1cm} 105 \hspace{1cm} 110$

Ser

<400> 37

Ser Pro Asn Pro Pro Asn Leu Thr Lys Lys Met Lys Lys Ile Val Asp 1 5 10 15

Ala Val Ile Lys Tyr Lys Asp Ser Ser Ser Gly Arg Gln Leu Ser Glu 20 25 30

Val Phe Ile Gln Leu Pro Ser Arg Lys Glu Leu Pro Glu Tyr Tyr Glu 35 40 45

Leu Ile Arg Lys Pro Val Asp Phe Lys Lys Ile Lys Glu Arg Ile Arg 50 60

Asn His Lys Tyr Arg Ser Leu Asn Asp Leu Glu Lys Asp Val Met Leu 65 70 75 80

Leu Cys Gln Asn Ala Gln Thr Phe Asn Leu Glu Gly Ser Leu Ile Tyr 85 90 95

Glu Asp Ser Ile Val Leu Gln Ser Val Phe Thr Ser Val Arg Gln Lys 100 105 110

Ile Glu

<210> 38 <211> 113

<210> 37

<211> 114 <212> PRT

<213> Homo sapiens

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<212> PRT
<213> Gallus gallus
<400> 38
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Ser Pro Asn Pro Pro Lys Leu Thr Lys Gln Met Asn Ala Ile Ile Asp 1 10 15

Thr Val Ile Asn Tyr Lys Asp Ser Ser Gly Arg Gln Leu Ser Glu Val 20 25 30

Phe Ile Gln Leu Pro Ser Arg Lys Glu Leu Pro Glu Tyr Tyr Glu Leu 35 40 45

Ile Arg Lys Pro Val Asp Phe Lys Lys Ile Lys Glu Arg Ile Arg Asn 50 55 60

His Lys Tyr Arg Ser Leu Gly Asp Leu Glu Lys Asp Val Met Leu Leu 65 70 75 80

Cys His Asn Ala Gln Thr Phe Asn Leu Glu Gly Ser Gln Ile Tyr Glu 85 90 95

Asp Ser Ile Val Leu Gln Ser Val Phe Lys Ser Ala Arg Gln Lys Ile $100 \hspace{1cm} 105 \hspace{1cm} 110$

Ala

<210> 39 <211> 114 <212> PRT <213> Gallus gallus

<400> 39

Ser Pro Asn Pro Pro Asn Leu Thr Lys Lys Met Lys Lys Ile Val Asp $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Ala Val Ile Lys Tyr Lys Asp Ser Ser Ser Gly Arg Gln Leu Ser Glu 20 25 30

Val Phe Ile Gln Leu Pro Ser Arg Lys Glu Leu Pro Glu Tyr Tyr Glu 35 40 45

Leu Ile Arg Lys Pro Val Asp Phe Lys Lys Ile Lys Glu Arg Ile Arg 50 60

Asn His Lys Tyr Arg Ser Leu Asn Asp Leu Glu Lys Asp Val Met Leu 65 70 75 80

Leu Cys Gln Asn Ala Gln Thr Phe Asn Leu Glu Val Ser Leu Ile Tyr 85 90 95

Glu Asp Ser Ile Val Leu Gln Ser Val Phe Thr Ser Val Arg Gln Lys
100 105 110

Ile Glu

<210> 40 <211> 105 <212> PRT <213> Homo sapiens

<400>

Ala Lys Leu Ser Pro Ala Asn Gln Arg Lys Cys Glu Arg Val Leu Leu 1 10 15 Ala Leu Phe Cys His Glu Pro Cys Arg Pro Leu His Gln Leu Ala Thr $20 \hspace{1cm} 25 \hspace{1cm} 30$ Asp Ser Thr Phe Ser Leu Asp Gln Pro Gly Gly Thr Leu Asp Leu Thr 35 40 45 Leu Ile Arg Ala Arg Leu Gln Glu Lys Leu Ser Pro Pro Tyr Ser Ser 50 60 Pro Gln Glu Phe Ala Gln Asp Val Gly Arg Met Phe Lys Gln Phe Asn 70 75 80 Lys Leu Thr Glu Asp Lys Ala Asp Val Gln Ser Ile Ile Gly Leu Gln 85 90 95 Arg Phe Phe Glu Thr Arg Met Asn Glu

<210> 41 <211> 105 <212> PRT

<213> Mus musculus

<400>

Ala Lys Leu Ser Pro Ala Asn Gln Arg Lys Cys Glu Arg Val Leu Leu $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ Ala Leu Phe Cys His Glu Pro Cys Arg Pro Leu His Gln Leu Ala Thr 20 25 30 Asp Ser Thr Phe Ser Met Glu Gln Pro Gly Gly Thr Leu Asp Leu Thr 35 40 45 Leu Ile Arg Ala Arg Leu Gln Glu Lys Leu Ser Pro Pro Tyr Ser Ser 50 60 Pro Gln Glu Phe Ala Gln Asp Val Gly Arg Met Phe Lys Gln Phe Asn 70 75 80 Lys Leu Thr Glu Asp Lys Ala Asp Val Gln Ser Ile Ile Gly Leu Gln 85 90 95

Arg Phe Phe Glu Thr Arg Met Asn Asp 100

<210> 42 <211> 108 PRT <213> Mus sp.

<400>

Thr Lys Leu Thr Pro Ile Asp Lys Arg Lys Cys Glu Arg Leu Leu 1 5 10 15

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Phe Leu Tyr Cys His Glu Met Ser Leu Ala Phe Gln Asp Pro Val Pro 20 25 30
Leu Thr Val Pro Asp Tyr Tyr Lys Ile Ile Lys Asn Pro Met Asp Leu 35 40 45
Ser Thr Ile Lys Lys Arg Leu Gln Glu Asp Tyr Cys Met Tyr Thr Lys 50 60
Pro Glu Asp Phe Val Ala Asp Phe Arg Leu Ile Phe Gln Asn Cys Ala 65 70 75 80
Glu Phe Asn Glu Pro Asp Ser Glu Val Ala Asn Ala Gly Ile Lys Leu
85 90 95
Glu Ser Tyr Phe Glu Glu Leu Leu Lys Asn Leu Tyr
100 105
<210> 43
<211> 27
<212> PRT
<213> Artificial Sequence
<223> synthetic bromodomain peptide
<220>
<221> MOD_RES
<222> (1)..(2)
<223> Any amino acid
<220>
<221> MOD_RES
<222> (4)..(6)
<223> Any amino acid; this range may encompass 2-3 residues
<220>
<221> MOD_RES
<222> (8)..(15)
<223> Any amino acid; this range may encompass 5-8 residues
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<222> (16)
<223> Pro, Lys or His
<220>
<221> MOD_RES
<222> (17)
<223> Any amino acid
<220>
<221> MOD_RES
<222> (19)
<223> Tyr, Phe or His
<220>
<221> MOD_RES
<222> (20)..(24)
<223> Any amino acid
<220>
<221> MOD_RES
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<222> (26)
<223> Met, Ile or Val
<400> 43
Xaa Tyr Xaa Xaa Xaa Xaa Xaa Asp 20 25
<210>
<211>
     20
<212>
      PRT
      Artificial Sequence
<213>
<220>
<223>
      synthetic bromodomain peptide
<400> 44
Trp Pro Phe Met Glu Pro Val Lys Arg Thr Glu Ala Pro Gly Tyr Tyr 1 5 10 15
Glu Val Ile Arg
20
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